

A STUDY OF ACUTE INFECTIOUS PROCESSES IN BONE.¹

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WITH the introduction of modern methods of biological research, the study of surgical pathology has made a vast stride from the domain of empiricism toward that of true science. It is not too strong a statement if one claims that, in the light of results obtained from bacteriological researches, our whole literature of general and surgical pathology must be rewritten, or so much of it as was published previous to 1885. I do not mean hereby to assume that our present position is in many respects an absolutely stable one, but that our knowledge gained previous to 1885 has been so enriched and extended that it must enjoy a new presentation in order fairly to represent the subject.

Let me not appear, while making such assertions, in an attitude too easily assailed. I am not in sympathy with the class of enthusiasts who are represented (and perhaps misrepresented) as considering bacteriology and pathology as synonymous, or who hold to *bacterio-centric* views, if I may coin the term. Nevertheless, I feel that we stand to-day where we can state without successful contradiction that the introduction of bacteriological studies and methods has revolutionized the principles, as well as the practice, of surgery, and that to their general acceptance is due its *renaissance*.

And now, with this general introduction, permit me to ask attention to a class of surgical diseases whose acquaintance was long since made by the clinician, but whose intimate nature, whose etiology and pathology, it has remained for the bacteriologist to clear up. I allude particularly to acute suppurative periostitis and acute infectious osteomyelitis—the names by which they are best known in this country. Terribly severe in their typical forms, often fatal, bringing dread and despair to patient and surgeon alike, causing the one to endure the torments of the damned and the other often to curse the utter helplessness of his measures, they have been at once the enigma and the stigma of surgery.

But this is no longer the case. Their etiology is now well known; the numerous changes which take place both inside and outside of the bone are pretty well understood, and only the connecting links between easily recognized trains of events are now concealed from our appreciation. And all this has been made possible by modern bacteriological and microscopical technique.

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Acute osteomyelitis and acute suppurative periostitis are, like tuberculosis, erysipelas, anthrax, and numerous other diseases, infectious maladies which develop under the influence and after the introduction into the system of one or more definite microorganisms. For manifestation of their pathogenic activities they undoubtedly need a predisposing condition of the system, but they are themselves the determining causes. For the recognition of this last fact we are indebted to the bacteriologists. For a demonstration, or further evidence, that they enter through some open pathway, through some lesion revealed or concealed, we must needs study our cases more carefully. We must realize that these conditions may have their origin, for instance, from an ulcerated tooth, or from some other lesion equally easily overlooked.

It is my desire to direct attention to the pathological, rather than the clinical or therapeutical aspect of my subject; and, furthermore, not so much to matters of gross pathology as to the most recent investigations into the truly parasitic nature of these diseases. To this end, let me at once take the position that without the presence of pyogenic bacteria we have no pus; a position which to-day needs no defence.

With this statement for a foundation, it shall be our task to try to make clear the biological position of the parasites to whose pernicious activity these disturbances are due, and to bring out such facts regarding their ports of entry, methods of development, and habits, as time may allow.

Questions to which we particularly need unequivocal answers, are:

- I. Is there a specific coccus of infectious osteomyelitis?
- II. Can more than one microbe produce it?
- III. How does any bacterium which can cause it effect an entrance into the system?
- IV. What influences do previously existing diseases exert?
- V. Is there possibility of a mixed infection in these cases, and in what does it consist?

Before attempting to answer these questions, let us secure a little help from a brief historical sketch of the matter.

HISTORY.—As Ivanoff has put it, "Between 'growing pains,' so called, which disappear after a few hours of repose, and the intensely agonizing acute osteomyelitis, which has been so justly styled *typhus des membres*, there are very wide differences." Under this name, acute osteomyelitis, more than one form of lesion has been described, while to the milder form different writers have given a variety of names. Schutzenberger, in 1853, was perhaps the first to call attention to this disease under the name of *rheumatic periostitis*, but during the same year Chassaignac carefully studied the disease and gave it the name by which it is now known. He presented to the Academy of Sciences a classic memoir upon this subject, and, in 1854, another to the Society of Surgery upon "Acute Subperiosteal Abscesses." While he recognized a wide distinc-

tion between them, he saw also that the two diseases presented certain points in common. In 1858 Becker described the same malady under the name of *phlegmonous periostitis*. Almost at the same time Klose published thirteen cases of this character under the name of *meningo-osteo-phlebitis*. In these cases he observed epiphyseal separation. About the same time, too, Gosselin published a memoir and described the disease under the name of *epiphyseal ostitis of adolescence*. In 1862 Gamet published a thesis which he entitled "Juxta-epiphyseal Osteo-periostitis." Others also gave it yet other names, among which was that of Giraldes, who usually spoke of it as phlegmonous periostitis. In 1878, Lannelongue published his classical memoir, describing it under the name of acute osteomyelitis of adolescence. It is rather with the acute and suppurative form that we have to deal, consequently I will not follow the history of the recognition and identification of the subacute or more chronic forms.

The gravity of the disease has long attracted the attention of surgeons. Searching for the causes thereof, Recklinghausen, Klebs, and others, examining the different organs of patients dying from the disease, found, in 1874, a micrococcus which they met with in the muscles, heart, pericardium, kidneys, and elsewhere, and which they considered the pathogenic agent, and upon whose recognition they founded various theories—some considering it the specific cause of the disease, others denying it.

Kocher attempted in a systematic, experimental manner to establish the parasitic origin of the disease. He injected various foul and putrid materials, and sometimes succeeded in setting up the trouble, and sometimes he failed. His materials, however, were not derived from pure cultures. Some of them, therefore, must have contained the specific microbes by accident. His conclusions were suggestive rather than conclusive.

In 1880 Pasteur, examining pus from a case of this kind, found also micrococci, which he cultivated, but with which he did not experiment upon animals. In 1881 Schüller, examining a limb amputated on this account, found the same organism in the bone, the periosteum, and the articular cartilages; but Becker was perhaps the first, in 1883, to report complete investigations with these organisms. He isolated and cultivated them upon various media, and then experimented with them upon animals. Injections of these cultures into the abdominal cavity produced peritonitis, but no trace of the lesion. He then made various contusions and fractures subcutaneously, and afterward injected these cultures into the veins; by this means he evoked the ordinary anatomical signs of osteomyelitis. He found them also in the lungs and kidneys, and concluded that he had to deal with a specific cause for the disease. Rosenbach repeated the experiments of Becker and elaborated them. He produced suppuration in the injured bones of animals after having

injected into their veins putrid material or cultures of lactic ferments, consequently he attributed small value to Becker's results. He made cultivations of the same cocci which others had studied and, with Ogston, gave to them the names by which we now know them. It was in 1881 that he cultivated the staphylococcus from the pus of a case of osteomyelitis. In one case he found both the albus and aureus combined; in another the albus alone; and in a third the aureus and streptococcus were found together. He produced the same result by injecting a pure culture of pyogenic microbes from a furuncle of the lip as Struck did with cultivations from osteomyelitic pus.

Krause, in 1884, cultivated from osteomyelitic pus *Staphylococcus aureus* and *albus*, which he found also in the effusion of the joints, occurring as a complication of this disease. He stated that when a bone was fractured subcutaneously, after the injection, he usually observed suppuration at the seat of the fracture, and from this pus the staphylococcus could again be cultivated. He endeavored further to produce a malady analogous to osteomyelitis without effecting such osseous injuries upon the animals. He was forced to the conclusion that there exists a coccus, in cases of acute infectious osteomyelitis, of extraordinary pathogenic and pyogenic powers, which, introduced in sufficient quantities, produces in animals acute infectious disease that leads inevitably to death, and which localizes itself by preference in the organs of locomotion, muscles, joints, and bones. His investigations were corroborated by Garré, who in addition showed that the staphylococcus is also present in such cases in the blood.

Ganglophe and Rodet, experimenting in the same direction, came to nearly the same conclusions, agreeing in the description of the microbes especially at fault; and these are now everywhere recognized by their biological characteristics and everywhere described under the same names. Until recently, opinions have differed as to whether there was a specific germ of acute osteomyelitis alone, which did not manifest pathological properties in other directions, or whether this was a condition which might be called out according to circumstances by various forms. With regard to this question, we shall have more to say a little later.

Rosenbach selected the bone marrow for his experiments, principally for the reason that it is most completely protected from external influences, such as the penetration of exciting inflammatory agents from the skin, or, in fact, from any direction save the circulation. He demonstrated that neither mechanical injuries, comminution nor destruction of the marrow, nor such physical influences as the cautery or the electrical current, nor the action of chemical caustics, could produce a suppurative phlegmon in the bone marrow. He demonstrated further, on the contrary, that this medullary matter was extremely sensitive to the influence of infectious materials, or to rancid butter or products of decomposition,

any of which speedily evoked violent symptoms of septic inflammation. Krause made the further valuable observation that all the common changes noticed in muscles, kidneys, etc., which are met with in pyæmia are found as well in cases of acute osteomyelitis. He observed only those changes at the spot of his experimental fractures which were called forth or met with in cases of ordinary septic poisoning, with this difference, perhaps—that the marrow at the site of the experimental fracture was more extensively involved than after ordinary injection of septic material.

PATHOLOGICAL ANATOMY.—A most important fact was comparatively early established, largely by the French writers, that in acute osteomyelitis the disturbance begins in the neighborhood of the epiphyseal cartilage, and that by early operation (trephining) the presence of pus can be demonstrated in the interior of the bone before it can be found anywhere else.

In the Memoirs of the Society of Surgery, 1855, Gosselin expressed himself as follows:

"When a bone is seized with diffuse ostitis the marrow participates in the inflammation. This marrow becomes highly infiltrated with blood and its vessels congested, plastic material is exuded from these same vessels and a portion of its fatty and albuminoid tissue is mixed with blood . . . Such a mixture of hydrocarbons and albuminoids is certainly one whose putrefaction would most rapidly lead to putrid poisoning, and whose putrid products are situated in a peculiarly favorable position for distribution throughout the system."

Some of the French authors, in describing the appearance of the interior of the bone, in serious cases of this lesion, have spoken of the medulla as exhaling an odor of infection. Some, like Reynaud, have supposed this to be due to gangrene of the same; others, like Gosselin, believed it due to putrefaction of the albuminoid and fatty elements of the bone marrow. It would appear that both mean practically the same thing, and they dignify it with the term *osteomyelite putride*. Of course, this means, in effect, a mixed infection, the ordinary putrefactive bacteria having also found entrance; or it may be due to the presence of Rosenbach's bacillus pyogenes fetidus or saprogenes.

The macroscopic structure of the parts whose diseases we are studying has no small importance in our present investigation. No one has given this matter more attention than Ollier, and I may be permitted to quote one or two of his observations:

"The connecting cartilage is intimately adherent to the periosteum, with which it is continuous and blended at its circumference. This continuity is well seen in separations of the epiphyses, when the extremity of a diaphysis, separated from its cartilage, breaks through the ensheathing periosteum and protrudes through the tear in the midst of the muscles." (*Int. Enc. Surg.*, vi. 855.)

Suppurative periostitis is, strictly speaking, endoperiostitis, as Ollier has shown; that is, it is the deeper layer of the membrane which is mainly and principally involved, and the bone must, in consequence, suffer more or less. It may, moreover, be primary or consecutive.

It is probably the cases of endoperiostitis in which the presence of bacteria does not figure, which lead to the rare condition of *periostitis albuminosa*, where a ropy, transparent fluid is met with instead of pus. These are to be regarded as inflammations which have been preserved from bacterial infection. In one instance of this kind that I have met with, neither the microscope nor culture experiments revealed the presence of microbes:

"The activity of the subperiosteal elements explains how the internal surface of the periosteum is also frequently the point of departure for osseous inflammations, which may be limited or may extend. In the latter case they spread all around the bone, and may reach the medulla through the juxta-epiphyseal regions, bringing about those isolations of the diaphysis, or those more or less extensive necroses which so often necessitate our interference." (Ollier.)

Besides these well-known and now commonly recognized forms of parasitic osteitis and periostitis, there is yet another rare one, which, in 1883, Kiener and Poulet described under the name of *ostéite tuberculeuse aiguë envahissante et suppurée*; a species of tubercular osteitis, usually central, of such acuteness that it deserves to be regarded as coming justly within the province of this paper. The greater part of the epiphysis is rapidly invaded and the inflammatory disturbance is most intense. On section, the interior resembles a section of a mass of ice-cream, part vanilla and part raspberry. Small abscesses, even as large as an almond, of yellowish tint, are found in the bone. In the whitish parts the bony partitions are hard, thickened, and the medulla infiltrated with caseous products. The reverse obtains in the reddened areas. If a sequestrum reaches so far as a joint, it perforates the articular cartilage and may fall into the joint cavity, determining there, of course, a purulent and fungous arthritis.

Some time since, I had to disarticulate at the shoulder-joint an arm in which a most typical picture of this rare form of acute disease was presented. At each end of each long bone in the extremity existed the peculiar lesions above alluded to, in their most illustrative form. This was before attention had been called to this peculiar form of disease, and yet my record of the case at the time, and the bony specimens still in my possession, stamp it as a typical case.

Rodet was the first to produce osteomyelitis in animals without inflicting a trauma before or after the injection. This he did by practising intravenous injections. The purulent inflammation, which was usually circumscribed, was commonly located near an epiphysis; it seldom extended over a large portion of the shaft. In many cases diastasis

occurred, and frequently arthritis of the adjacent joint. In the most acute cases the animal died within twenty-four hours, with scarcely any change in the bone. The detection of microbes in the blood was the most difficult. They were most easily found in the kidneys, in which multiple abscesses were often met with. Subcutaneous injection resulted only in local infection; osteomyelitis could be produced only by intravenous injection. Young animals were the most susceptible. As the result of his observations, he considers the medulla, in close proximity to the epiphyseal line, as the primary seat of osteomyelitis of long bones. When epiphyseal separation occurred the pathological fracture was always on the side of the diathesis.

The explanation of these results is not difficult. Cocci may be carried directly to the vicinity of growing bone marrow by direct blood current, or they may be lodged upon a mucous membrane and here cause a local inflammation with local stasis, and then, after causing adhesion of infected leucocytes and local thrombosis, they may be carried along and lodged in some vessel too small to permit their passage. Should accident determine this to be in the bone, then we have the conditions under consideration as the result.

PREDISPOSING CAUSES.—In these cases as in every other acute illness, we find certain conditions of the system which we may consider as predisposing causes. Our most typical illustrations are met with in the adolescent, where, as is well known, there is a maximum of circulatory activity in the neighborhood of the epiphyses. It is not saying too much to claim that where we find the greatest nutritive activity we get our most disastrous results from sudden changes. Let these changes be produced by injury, even slight, or exposure or reflex influences, so that a certain stasis shall ensue, and we can then better imagine how, when once a comparatively small number of pyogenic cocci have gained entrance through the blood channels, they rapidly multiply, causing coagulation-necrosis, and become agents for the most active destruction and evil. Another anatomical fact is of great importance in this connection; the bone marrow is especially predisposed, in composition as in histological structure, to collect and retain germs of disease. It is, moreover, most sensitive in its reactions, and there is further to be considered its now well-known function in the perfect elaboration of the blood. When, therefore, it is attacked, not only is there local disease, but there may be readily brought about serious and rapid alterations in the blood and conditions of true toxæmia.

It is, furthermore, at the age of childhood, as Ollier puts it, "That the action of cold, forced exercise, fatigue of the skeleton, or juxta-epiphyseal strain, give rise, under the influence of a scrofulous or rheumatic predisposition, or of a general systemic poisoning, to those acute or subacute lesions," at points "where increase in length takes place,

and under the periosteum, where increase in thickness occurs." Almost all authors have recognized a predominance of this disease in the male sex. According to Lannelongue, out of one hundred and twenty-two cases, eighty-six were in boys and thirty-six in girls. Many writers unite in mentioning scrofula as a predisposing cause, and this must result not only from the cachexia or diathetic condition which the term scrofula implies, but also from the fact that active scrofulous lesions are tubercular lesions, and that the breaking down of tubercles in bones is a condition of mixed infection, which is simply intensified in activity and abbreviated in time in our most acute cases.

Privation and unhygienic surroundings play also a conspicuous rôle as predisposing to this disease. Whether acute articular rheumatism may be included in this category, is a question not yet settled. When we consider how rare suppuration is in connection with purely rheumatic affections, we may tentatively, at least, leave it out from further consideration.

We are justified in laying great stress on fatigue and exhaustion as predisposing causes.

It is not alone disease nor, in fact, any absolute diseased condition which predisposes to osteomyelitis; bad hygienic surroundings, as will be seen among the children of the poor in crowded cities, long forced marches, even lack of proper rest or of proper food, play almost as large a rôle as do actual injuries. The statistics of wounds among the insurgents of the Commune are sufficiently eloquent in this respect.

I am convinced, with Ollier, that hitherto we have not ascribed enough importance to the matter of juxta-epiphyseal strains in delicate and scrofulous children, as an active factor in producing acute suppuration of the parts. These are produced by falls, or by violent movements, which may be easily overlooked or forgotten. Minute separations, trabecular fractures or hemorrhages are thus caused, which suffice, together with the vulnerability of the system so well recognized in such children, to lead to extensive disaster.

He (Ollier) speaks of the extension or migration of the inflammatory disturbances alluded to from one end of the diaphysis to the other, along the periosteum or medullary canal, sometimes without stopping, and going on to suppuration at both extremities of the shaft, so that we have to deal with two distinct centres of suppuration; and he denominates this *bipolar ostitis*. This is especially common in the tibia, and, I doubt not many of you, like myself, have seen repeated instances of it.

Some French writers have spoken of pericarditis as a predisposing cause. In the writer's estimation, this is more likely to have been either a coincident lesion or a consequence, since the same bacteria are involved in each case. The same may be said of endocarditis. The most active occasional causes are strain, exposure, or excessive fatigue, or all three

combined, especially if occurring in a patient with a tuberculous taint or diathesis.

Inasmuch as the extremities usually suffer most from these causes, it will be seen how easily such circulatory disturbances as partial or complete stasis may be thereby brought about, and how many organisms circulating in the blood may most easily find here a suitable culture-medium, surrounded by fewest disturbing elements. The French surgeons, especially, discussing this topic have shown considerable acerbity as to whether the periosteum or the medulla is first involved. This seems to have been quite unnecessary, if we remember that the bone marrow extends in effect to the very surface of the bone. After all, it is a matter of very trifling importance; inflammation begins at either point, extends rapidly to the other, and, in our worst cases, we have to deal practically with a phlegmonous peri-osteo-myelitis.

Osteomyelitis rarely affects short or flat bones; one meets with very few such cases. There is during the growth of long bones a concentration of nutritive activity, which within certain limits is intense; a concentration made necessary by the necessity for their growth mainly in one direction—that is, length. This growth of long bones in one direction is characterized by a great vascular richness, by a most active proliferation, by much energy in young tissues which are quite delicate, and which are subject to invasion by infectious agents. This may figure as the sole factor in producing acute osteomyelitis, and, though these infectious agents have the power of determining an explosion of disease, as it were, still we cannot be blind to the fact that their activity is prompted alone by the alterations which are so rapidly taking place in the ends of the young bones. The short and flat bones, as well by their situation as by their function, are much less exposed to these alterations; their centres of ossification are not as localized, while ossificatory activity is much milder and less susceptible of deviation.

We are forced to recognize, moreover, cases of acute inflammatory disturbances upon the articular side of the epiphyseal line. In this case care will be required to discriminate between an acute suppurative synovitis and an acute infectious epiphysitis. Inasmuch as intense pain and tenderness, with muscular spasms, will generally predominate early in the latter case, we shall not have much difficulty in this respect. Epiphyseal separations have occurred in cases where this disaster has been veiled in the general features of an acute pyarthrosis.

In a recent thesis Lemoyne has summed up certain conclusions which may be appropriately reproduced here:

“First, that acute suppurative inflammation is frequently met with; second, that it is manifested in two forms, either as phlegmonous periostitis more rarely, or as acute osteomyelitis more commonly; third, that the disease is of an infectious nature, the causes formerly evoked not being sufficient to

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explain its development; fourth, that the symptoms in the adult are quite analogous to those in children; fifth, that when inflammation is limited to the deeper layers of periosteum recovery is more likely without necrosis or exfoliation; sixth, that the reparative process is often followed by more or less hyperostosis; seventh, that the prognosis is more grave after the individual has reached the twenty-fifth year of life."

As illustrating the rapidity with which destructive processes may take place, let me quote the following statement by Ollier, made at the first Congress of French Surgeons:

"Rodet has been able to reproduce all the varieties of juxta-epiphyseal ostitis by inoculations with fluid cultures of the *Staphylococcus aureus*. I have had opportunity to examine some of the specimens thus obtained, and in some of them have been able to demonstrate the presence of a sequestrum even so early as two or three days after inoculation."

The usual form of lesion observed by Rodet was rarefying; exceptionally it was condensing.

A case reported by Gerster shows that extensive necrosis may take place in three days after the inception of the disease. He believes, as I do, that a few hours are sufficient to determine its occurrence. Perhaps the most rapidly fatal case on record is that reported by Kohts, in which the disease began and ended apparently in thirty-six hours. (Right femur involved.) The reporter regarded the peri-bronchial tissue as the port of entry in this case. Most painstaking investigation revealed fat-embolism of the lungs, pulmonary infarcts, purulent peri-bronchitis, "myositis mikrocoecica;" bacteria were found, as well, in the capillaries of the spleen and kidneys. The peri-bronchitis in this instance was ascribed to a tumble into the water which had befallen the child three weeks previously.

The complications of acute infectious disease in bone are mainly in the direction of septicæmia and pyæmia, except so far as local destruction is concerned. If circumstances permit a reasonably early escape of pus, the final septic disaster may be averted. When this does not occur, and when the surgeon fails to effect an escape of pus and relief of tension, a patient is pretty sure to die of pyæmia. If we are right in speaking of these cases as in the first place a local pyæmia of bone, we shall more readily understand how easily and naturally this result is brought about. As Verneuil has put it:

"Lesions of bone are predisposed especially to severe septicæmia. They prompt and favor continuation and prolongation of dosage of putrid poisoning. The poisonous material is shut in in such a way that escape by way of the vessels and final circulation is almost impossible."

Accepting this view, we can understand both the justness of P. Wagner's expression *kryptogenetische Pyämie* as furnishing a clew to the concealed origin of some previously inexplicable cases of idiopathic pyæmia, and of Leube's *spontané Septiko-pyämie*.

Indeed, the view that acute osteomyelitis sustains a close relation to pyæmia is hardly expressing it strongly enough. It not only leads to pyæmia, but it is, almost from the beginning, a pyæmia. This is to be explained, of course, on the anatomical ground that osteomyelitis is essentially a septic phlebitis of bone marrow, and when we remember the most important rôle played by the veins in the production of the pyæmic condition, we can see how almost immediately an osteomyelitis, regarded in this light, becomes first a local and then a general pyæmic condition.

THERE IS NO SPECIFIC GERM OF THE DISEASE.—Osteomyelitis is, in the light of these and other facts to be adduced, not to be regarded as a specific disease, but as one manifestation of the pathogenic properties of several microorganisms possessing common specific pyogenic activities. It is a phlegmon of bone, or a local pyæmia.

Experiments to ascertain the extent of diffusion of an osteomyelitic microbe have been made by Ribbert. Twenty-four hours after direct injection he found them in all the organs; but later, only in the kidneys. In regard to their localization, three conditions must be taken into consideration: *First*, embolic obstruction of capillaries; *Second*, elimination of pyogenic cocci through the kidneys; *Third*, influence of traumatism. Lübbert entered into a most careful study of the alleged coccus of osteomyelitis, and established for himself its complete identity with the *Staphylococcus aureus*. His monograph also demonstrates the diversity of the lesions caused by this organism. He further showed that *en masse* it was more resistant to elevated temperatures when dry than when suspended in water. When dry it withstood a heat of 80° C. (176° F.) for nearly an hour. Like many other pathogenic microbes, the more it is cultivated in living animals, the more intense, apparently, becomes its activity.

From his biological study, Lübbert was led to the conclusion that the intensity of action of the *Staphylococcus aureus* varied greatly without sufficient cause of variation being known. Inoculation of granulation surfaces proved harmless; even on superficial abrasions it seemed to produce no effect. Subcutaneous injections resulted in the formation of abscesses of varying degrees of severity. Injections into the pleural and peritoneal cavities were oftenest followed by intense symptoms; intratracheal injections produced suppurative tracheitis and foci in the lungs; intravascular injections were followed by septic symptoms, with foci in the intestinal mucosa. Feeding experiments proved harmless. Why the staphylococcus forms should at one time produce a superficial abscess, at another a deep and disastrous phlegmon of bone, and at yet others an endocarditis, a pericarditis, a brain abscess, a purulent synovitis, or any one of many other manifestations of its presence, we can, as yet, only partially answer. When we can formulate an accurate response to this

query we can tell, also, why rarely a subcutaneous fracture suppurates, or why, as in an instance related by Bergmann, a piece of cloth encapsulated in the deeper tissues for fifteen years should finally set up a typical abscess.

Bertoye came to the conclusion that the *S. albus* was less malignant in its action in bones than the *S. aureus*. He thought, moreover, that *S. albus*, after a series of cultivations through living animals, gradually became converted into the other variety, *i. e.*, *aureus*.

Garré's experiment of applying a quantity of pure culture of *S. aureus* taken from a case of osteomyelitis to the unbroken skin of his own arm, and thereby producing a typical carbuncle, shows how it is not always necessary to invoke the hypothesis of a precedent lesion in order to explain the occurrence of a deep-seated phlegmon.

Kraske has also had opportunity to observe a case illustrating the same identity between the microbes met with in osteomyelitis and carbuncle.

The writer's own studies of a few carbuncles have shown him that the *Staphylococcus aureus* is almost always to be met with in this affection, along with other cocci. Out of five cases of osteomyelitis bacteriologically studied by Kraske, the *Staphylococcus aureus* was twice found alone; in the other cases other species were also met with; some of these forms being present probably by accident, and some of them presenting forms not yet identified, whose consequent pyogenic importance is not yet recognized. Kraske takes the ground that the somewhat various features and courses pursued by different cases of osteomyelitis may be, in some degree, at least, owing not only to the presence of the various pyogenic cocci or to their contamination with other forms, but also to the various ways in which infection may have occurred.

A complete recognition of the absolute etiological identity of acute spontaneous and acute traumatic osteomyelitis can only be insisted upon after extensive bacteriological investigations. It may make a difference as to whether the microbe is introduced directly into the bone, as in injury, or by bloodvessels, as in the idiopathic forms. The character of the inflammation may also vary according to the culture medium in which the germ lodges, just as it makes a difference in laboratory experiments whether one makes a needle or a plate culture.

Kraske considers that recurring attacks are not necessarily an indication of former infection, but may arise entirely *de novo*. The results of his clinical studies are, first, the *Staphylococcus aureus* can produce osteomyelitis, and is in fact most frequently met with in osteomyelitic products; second, in a certain number of cases acute osteomyelitis is the result of a mixed infection, and is then most prone to produce a severe case. He thinks that the localization of cocci in the neighborhood of epiphyseal lines in young persons is due to the peculiar location and

arrangement of the capillary vessels in this neighborhood, and that, almost without exception, the inflammatory process has its origin here; that the rapid local spreading of the disturbances is in large measure due to the unyielding nature of the tissues around the primary trouble, and to the fact that the bloodvessels act as direct disseminators, their contents forming the nutrient material for the microbes. Thrombosis is a coincident and necessarily very early condition in every case of acute osteomyelitis. When the microbes reënter the unobstructed vascular channels again, we generally get dissemination and metastatic foci, with coagulation-necrosis of the intima and thrombosis locally. As is well known, in some cases, even of external infection, early in the disease the constitutional symptoms are entirely disproportionate to the local lesions, giving us a clinical picture of intense septic intoxication. This is in all probability an acute ptomaine poisoning, which may possibly be due in its rapidity and intensity to the character of pabulum furnished by medullary tissue.

From some of my own cases that I have tried to investigate carefully I can report the following findings:

I. Case of acute lumbar disease, running a rapid course and terminating in abscess and caries. Found only the *Staphylococcus pyogenes citreus*.

II. Case of acute central osteitis of humerus. Found *Staphylococcus pyogenes albus* and *aureus*.

III. Case of acute necrosis of tibia, following osteoperiostitis. Found *Staphylococcus pyogenes aureus* and *cereus flavus*.

IV. Case of bone abscess of the femur following acute juxta-epiphyseal osteomyelitis. Found *Staphylococcus pyogenes aureus* and *cereus flavus*.

V. Case of acute central osteomyelitis of clavicle, resulting in nearly total necrosis. Found *Staphylococcus pyogenes albus* after cultivation, and tubercle bacilli in the pus, *i. e.*, mixed infection. This case (child) I had operated upon before, having removed the entire lower jaw (a half on each of two occasions) for trouble of similar character.

VI. Case of acute and rapidly fatal osteomyelitis of femur in a young girl. Amputation at hip-joint in desperate attempt to save life. Found *Staphylococcus pyogenes aureus* and *Streptococcus pyogenes*.

VII. Case of acute osteomyelitis of tarsus, with extensive destruction of the same. Found *Staphylococcus pyogenes aureus*.

It falls to my lot to see many cases similar to those above reported, but circumstances have either prevented any examination of the others or my results have seemed not quite worthy of reliance.

The view that each of these conditions is due to a distinct specific form is now well nigh abandoned. For my own part, I have, in a case of puerperal septicæmia, accompanied by ulcerative endocarditis and multiple but apparently not metastatic abscesses, many of them subperiosteal,

recognized the *Staphylococcus albus* by careful culture experiments; consequently I record it as but another expression of specific infection in connection with acute deep phlegmon. We meet also with acute endocarditis which may or may not be fatal. Just such cases have not presented in my own experience, but one may find them recorded, as, for instance, in the thesis of Benoit (Paris, 1876, No. 308).

It is now generally agreed among pathologists that the staphylococci are the causative agents not only in pus production, and its various manifestations as seen in the periosteum and the bone, but also in the production of acute ulcerative endocarditis, as well as of most of the other suppurative disturbances met with in these cases. Furthermore, that they, probably with the streptococci, are at fault when we have to deal with septic infection, whether it appears as sapremia, septicæmia or pyæmia, and whether it occur apparently spontaneously, or in the puerperal state, or in any other form. I think we may say that we do not at present know a form of this septic infection which can be separated from the presence of these organisms.

STAPHYLOCOCCUS RE-INFECTION.—There seems to be no denying the fact that collections of pyogenic and pathogenic organisms can shut themselves off in certain parts of the system where, as isolated cells of low formation, they remain quiet for months or years until called into activity by some new or special provocation. It is not overstating the matter to claim that isolated collections of pyogenic cocci remain quiescent for long periods of time, especially in the bones, even for twenty years, or longer, then to break out again, as it were, into a conflagration, when anything happens that may permit the outbreak; prolonged exposure, dissipation, or overexertion may bring this about; so may such wasting diseases as typhoid; so may also pregnancy, the puerperal state, puerperal fever, or any other local infection, and so may also such injury as a fracture. There is nothing stranger in all this than that it is strange that grains of corn or wheat may be kept for decades or centuries and then, under favorable auspices, once more resume cell activity and cell proliferation. This statement finds many clinical illustrations, as when we have occasion to remove sequestra from limbs which show many old scars of old bone abscesses, or when we even have to amputate for destruction too extensive to permit milder measures.

In fact, in most cases of osteomyelitis in the adult we shall find, as Lannelongue has told us, vestiges of similar trouble dating back to childhood or infancy.

I have recently had in my own practice a case where I had to amputate a thigh for acute necrosis, resulting from acute osteomyelitis, where the last outbreak of bone trouble of which I could get any account dated nearly twenty years previous. I feel as confident with this case as I do with anything which I cannot demonstrate, that a collection of

microbes of years' standing had been excited into activity as the result of overexertion and prostration. So, too, Volkmann says:

"I have already observed five or six cases where patients who had suffered from acute periostitis or osteomyelitis, and who exhibited extensive bone scars, have been suddenly seized after ten, fifteen, even twenty years, with acute diffuse inflammation which proceeded from their previous disease, and exhibited a peculiarly severe destructive character. Four of these patients died; two of them of acute pyæmia; in one case amputation of the thigh was necessary."

Gerster has reported a case of apparent quiescence of forty-seven years between the attacks, the disease recurring after this period at the same spot.

Rosenbach emphasizes the comparatively long period of time during which cultures remain active, and calls attention to the clinical manifestations of this fact in that suppuration may be resumed in bones, at points where previous lesions had existed, long after the original disease had apparently subsided.

Were it worth while, I could give many other illustrations of this clinical feature from my own practice, including several in which limbs have had to be removed to secure relief.

Kraske makes the important point that by no means every case of recurring osteomyelitis is really such; quite a large proportion of them depend upon a new infection, determined by certain changes in the bone marrow, which later, at an age when the disease is most common (period of youth), predispose to fresh inoculation. The rest of these cases undoubtedly are connected with the long period of quiescence to which I have already alluded.

PORTS OF ENTRY.—Observers have long noted the coincidence of osteomyelitis with various excoriations, abrasions, wounds, and superficial or deep lesions, but without drawing, until lately, the conclusion that the osteal lesion was the result of infection through these channels. Chassaingnac was the first to trace a causative relation, as he did in the case of a boy whose ankles had been chafed by his boots and who had a very severe osteomyelitis of the right femur. Several of the earlier observers in this direction have remarked their cases occurring in those who have recent or older scars. Camps has called attention to the fact that in cases involving the phalanges small lesions about the fingers have usually preceded. And so osteomyelitis of the lower jaw frequently follows some local affection, usually from inside the mouth.

A point of the greatest importance, therefore, is to recognize, if possible, the path of infection. As we understand it to-day, infection may occur through the skin, through the respiratory and circulatory organs, through the mucous membrane or intestinal canal, and through injury by direct penetration.

It is more than possible that the source of infection in acute osteo-

myelitis may be a suppurative focus upon or just beneath the skin, and that this, even, may be so minute as to be unrecognizable. A furuncle of the lip has been known to be the exciting factor in such cases as this.

In fact, Kraske is of the opinion that in the majority of cases the infection proceeds from the skin or the subcutaneous areolar tissues. Kocher had already called attention to his so-called secondary osteomyelitis, and the fact that in seeking for its cause one must not forget to examine carefully the entire surface of the body, and next to this the lymph glands, just as in a large portion of the formerly so-called "scrofulous glands" one could discover almost always some epithelial defect through which infection could take place, and from which swelling and suppuration of the glands ensued.

It is important in this connection not to overlook the tonsils as the possible seat of infection, since more than one observer has found their tissues more or less loaded with the *Staphylococcus aureus*, and Kraske considers it quite possible that a general infection may follow the growth of staphylococci in these glands.

The recent thesis of Ayala-Rios contains some carefully reported cases showing how osteomyelitis has followed, in one case, chilblains; in a second, felon; in a third, chafing and abrasion of the scrotum and groin; in a fourth, abscess; injury to head in a fifth; chafing and lymphangitis in a sixth; and furuncle, aphthous ulceration of the mouth, and other ordinarily mild and superficial bruises or lesions in yet others. In seven (*i. e.*, one-half) of his cases the serious osseous disturbance seemed to be in close relation—in point of locality—with the point of entrance of the microbes; in the other seven this close relation did not obtain.

Gerster has reported a case of extensive rapid destruction of one ischium with extensive purulent infiltration, the patient having had chronic suppuration in the middle ear.

Kraske asks the question, "Is it possible or probable that osteomyelitic infection may result from the alimentary tract?" Kocher has been decidedly of the view that this is possible. The infrequency of such infection is, of course, only negative. We know that both anthrax and tuberculosis can be produced by the ingestion of infected food. The peculiarity of Kocher's experiments may, perhaps, prevent us from completely accepting his views, and yet we cannot contradict the evidence of his two cases, in which he seems to show clearly that the intestines were the source of infection. We are in position, then, rather to say that the intestine is a possible source of infection than that it is a well-known source. Much more probable is infection through the lungs, and, consequently, the circulation. We are as well aware, of course, of the transfer of organic cells as of inorganic material from the respiratory organs to the bronchial glands; this being the fact, the general or more distant local infection is generally a difference in degree.

In a case of acute osteomyelitis two paths of exit are open for the pus: one by way of the joint, the other through the periosteum—the latter being the more frequent. It is, in fact, cases of the latter variety, where the pus forms in the middle of the long bones, which have led to the error of mistaking many of these for cases of simple acute suppurative periostitis. Such a case will be presented to a surgeon for the relief of what is supposed to be a simple subperiosteal abscess with, perhaps, superficial caries, but which will be found to be a case of deep central lesion. In the past few weeks a young lad was brought to my clinic whose case had been regarded as simply one of acute periostitis. I learned that he had suddenly been seized, in September of last year, with severe pain in one leg, which rapidly became intense. His case was for two or three weeks a very serious one; his fever was high, he was delirious much of the time, and even his life was despaired of. Later fluctuation was detected, a small skin opening was made, and pus evacuated. After this his most urgent symptoms subsided. When brought to me, the latter part of March, I found four sinuses, near the middle of the tibia, discharging small quantities of pus; upon operation it was found that nearly total central necrosis had taken place, and it was necessary to remove, subperiosteally, nearly all the bone from one epiphysis to the other. Surely, no ordinary case of periostitis alone could bring about such deep and central destruction of bone as this case presented.

This was an illustration of perforation of pus through the periosteum; on the other hand, we find either epiphyseal perforation with formation of extra-articular abscesses, or direct perforation of pus into the joint, with consequent necrosis and destruction of more or less of the joint structures, and permanent loss of function providing that life be spared. The discovery of pus in a joint-cavity, in such cases, is not necessarily a sign that it has perforated from the medullary cavity. It may be empyema of the joint consequent upon the presence of pus in the neighborhood, as we find ordinary empyema after acute specific process in the lungs proper, or it may be an expression of a metastatic process, in which case other manifestations of the same will probably be detected.

MIXED INFECTION.—We have two forms of mixed infection complicating acute suppurative changes in bone and periosteum, which certainly deserve brief special consideration. These comprise the typhoid and the tubercular. Whether the syphilitic properly may form a third we cannot yet say. The tubercular form I have already alluded to when speaking of the clinical manifestations described by Kiener and Poulet. Not less interesting are the acute disturbances in bone consecutive to typhoid.

Ponfick's researches concerning sympathetic affections of bone marrow after internal disease constitute most interesting reading, and are well worthy of study in this connection. They show how a large number of

infectious diseases such as typhus, typhoid, intermittent fever, continued fevers and the like, determine changes in the bone marrow which are anatomically recognizable. This being the case, we can easily see how slight a provocation in the way of septic infection is necessary to set up acute and disastrous suppurative changes.

Typhoid bacilli have been found at wide distances from the intestinal canal; Gaffky has found them in the liver; Bouchard has met with them in the urine and in the kidneys. They have been found in hyperæmic lungs along with other bacterial forms. They have also been seen in connection with other lesions in furuncles, in bedsores, and in connection with other septicæmic lesions.

Whether the specific bacillus of typhoid is properly to be ranked with the true pyrogenic bacteria, or whether its lodgement and the changes incident thereto simply predispose to a mixed infection with the staphylococcus or streptococcus, is a question, in my estimation, hardly yet to be positively answered. I do not forget that, for instance, Fränkel in 1885 carefully studied a case of post-typhoid abscess of the abdominal wall, from the pus from which he cultivated typhoid bacilli and these only. His case certainly demonstrated that the typhoid microbe could remain in the body longer than was ordinarily supposed (four months in this case), and it would seem to show that rarely it can manifest true pyrogenic properties; still, such an investigation needs confirmatory evidence.

Of no small interest in this connection is a recent paper by Ebermaier. (*Archiv für klinische Medizin*, Bd. 44, Heft 2.) In two cases of periostitis, occurring as a complication of typhoid fever, he was able to prove the presence of the typhoid bacilli in the pus and blood present. The first case was in an eighteen-year old lad, in whom, on the thirteenth day of the disease, signs of a periostitis of the second metatarsal bone of the left foot appeared. On the twenty-first day fluctuation was present, and the abscess was opened. Examination of the pus showed the presence of a few typhoid bacilli, and cultivation confirmed the microscopic result. The second case was in a nineteen-year old seamstress, in whom a periostitis of the right tibia developed during convalescence. The affected spot was incised; no pus obtained, but much blood. Cultivations obtained from this gave the typhoid bacilli. In neither were any other micro-organisms found. He gives six other cases of periostitis occurring during the course of typhoid fever, one of which went on to suppuration; he thinks that the results obtained from the first two cases allow us to consider the typhoid bacilli as their causative agent. He considers that the bacilli reach the periosteum from the medullary part of the bone through the Haversian canals, and is led to this belief from having obtained cultures of the typhoid bacilli from the medullary part of a rib removed post-mortem from a fatal case of typhoid fever. Whether

this affords all the evidence needed each one of us must determine for himself.

At all events, I can state of my own knowledge, not all post-typhoid abscesses contain such pure cultures of typhoid bacilli, since in at least one such case I have been able to cultivate the common *Staphylococcus aureus* from the pus, along with the bacillus in question.

Post-scarlatinal abscesses are certainly usually mixed infections, providing the alleged germ of scarlatina has aught to do with them, since in cases of this kind, too, I have found nothing but the common pyogenic forms, even after careful plating. When we know positively what micro-organism it is that produces scarlatina, we can speak with more certainty about mixed infection in this connection. So, too, with the other exanthemata. Rarely we hear of cases of acute bone trouble following after variola.

In the *Archives of Medicine* for 1830 (vol. iv. page 491) there was reported by Ancell a case of a babe of eleven months suffering with smallpox. An eruption appeared, discoloration commenced on the tenth day; upon the eleventh day the infant showed signs of distress; various swellings occurred in the neighborhood of the joints; fluctuation soon followed, with dilatation of superficial veins; fresh swellings appeared, crepitation was noticed in the joints and on pressing the fingers; even the costo-vertebral joints presented crepitant tumors. After death diastasis of most all of the epiphyses was noted, while the various joints were filled with pus.

In closing, let us now see to what extent we can answer the questions propounded at the beginning of this paper. I think we shall be perfectly safe in adopting the following conclusions:

I. There is no one specific microbe for the production of acute infectious processes in bone.

II. Most, if not all, of the staphylococci can cause them. Exceptionally, the streptococci may exert such an influence. So may tubercle bacilli and those of typhoid.

III. Commonly, when these latter are met with, we have to deal with a mixed infection, the pyogenic cocci being the final and active destructive agents.

IV. Of all forms, the *Staphylococcus aureus* is the most pernicious.

V. The parasitic infection may occur through the ears, eyes, nose, mouth, pharynx, respiratory passages, mucosa of the alimentary canal, or skin; or, in other words, through any lesion of the external or internal body surfaces. Furthermore, from any subcutaneous phlegmon, however small.

VI. The infection need not necessarily have been recent. The staphylococci and the bacilli of tubercle have the property of hiberna-

tion, so to speak, and their period of latency is one of almost indefinite length; this is especially true of the former.

VII. Some predisposing condition will be usually found to have favored the entrance of the infectious germs into the system and their lodgement in the localities where they manifest most activity.

VIII. Of the general causes which favor their entrance the diathetic conditions, such as the tubercular, and the dyscrasial, like the syphilitic, also the post febrile, play a most conspicuous part. Age, *i. e.*, childhood, is also always a predisposing cause.

IX. Of the causes which favor lodgement in particular localities, exposure, exhaustion, strain, and more marked traumatisms are those usually met with.

X. Pathologically, a case of acute infectious osteomyelitis becomes within a few hours a case of localized pyæmia, with all that the term implies; and this within a few hours more may become so generalized that a patient may die, even within thirty-six hours after noting the first symptom, of overwhelming septic intoxication.

XI. Acute infectious periostitis may run almost as acute a course, locally, as the same grade of osteomyelitis; but, inasmuch as pus finds more readily an outlet, it seldom leads to as rapid general disaster.

XII. A final conclusion in a therapeutic direction may, perhaps, be permitted here. No matter how former surgeons, like Demme and Chassaignac, disputed the matter, there is to-day but *one* safe and rational treatment, and that is, early and radical operation. These cases have been too often considered to be acute rheumatic affections, and many lives and limbs have been sacrificed to this diagnostic error. Our books and teachers need to give more exact instruction in this respect. When students are taught to recognize early the gravity of these conditions, they will learn that which, in many schools at least, they are not taught to-day. And now that we no longer dread as we did a combat with these insidious and invisible foes, there is no longer any reason for hesitating to operate early, since it offers our sole and almost only hope. Early, radical, and antiseptic attack constitutes, then, the therapy of the diseases to which I have invited your attention.

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CONGENITAL TUBERCULAR MESENTERIC DISEASE AND SUB-DIAPHRAGMATIC ABSCESS.

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THE comparative infrequency with which congenital diseases, other than syphilitic, are found, and the difficulty so often experienced in discovering in a subject so young the exact nature of any ailment from which it is suffering, and, in case of a fatal termination, in obtaining an